REMARKS

Reconsideration is respectfully requested. Claims 42-52, 54-64, and 66 are pending. Claims 1-41 and 53 have been cancelled. Claims 42, 45, and 49 have been amended. Support for amended claims 42, 45, and 49 can be found for example on page 45 lines 4-10. Claim 65 has been withdrawn. New claim 66 has been added. Support for new claim 66 can be found for example on page 46 line 33 through page 47 line 10.

With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Election/Restriction

The Examiner has withdrawn claim 65 as directed to a constructively non-elected invention by original presentation. Applicant has amended claim 65 to include all limitations of the apparatus of currently amended claim 42. Upon allowance of claim 42, Applicant requests rejoinder of claim 65. MPEP § 806.05(i).

Claim Rejections - 35 U.S.C. §102

Claims 45-47, 55-57, and 60-64 stand rejected under 35 U.S.C. §102(e) as anticipated by Lennox et al., U.S. Patent No. 6,461,490 ("Lennox") as defined by Morris C. ed (Academy Press Dictionary of science and Technology, Academic Press, San Diego, 1992, page 1726) ("Morris").

For an anticipation rejection under 35 U.S.C. §102 to be proper, a single reference must expressly or inherently disclose each and every element of a claim. In re Paulsen, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Lennox, as defined by Morris, fails to teach every limitation of the claimed invention. Without acquiescing or admitting the Examiner's position, and solely to facilitate prosecution on the merits, Applicant has amended claim 45 to require "a nucleic acid capture probe covalently attached to said electrode." Lennox fails to disclose this requirement.

Thus, it fails to teach every limitation of the presently claimed invention. Because it fails to teach all claim limitations, Lennox fails to anticipate the claimed invention.

Applicant respectfully requests that this ground for rejection be withdrawn.

Claim Rejections – 35 U.S.C. §103

Claims 42-44, 46-52, 54-58, and 60-64 stand rejected as unpatentable over Lennox in view of Anderson et al., US Patent No. 6,326,211 ("Anderson"). Claim 59 stands rejected over Lennox, as defined by Morris, in view of Anderson, and in further view of Hayes et al., U.S. Patent No. 6,334,980 ("Hayes").

35 U.S.C. § 103(a) requires that "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). The prima facie case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success.

1. The combined references fail to teach all claim limitations as required by the presently claimed invention.

As discussed above, Lennox fails to disclose "a nucleic acid capture probe covalently attached to said electrode" as required by currently amended claims 42, 45, and 49. Anderson also fails to provide such a teaching; instead, Anderson describes conventional preparation of oligonucleotides arrays. With respect to the rejection of claim 59, Hayes also fails to teach every limitation. As such, the references as a whole fail to teach the claimed invention.

2. The cited references fail to provide the requisite motivation or suggestion to modify their teachings and supply the missing claim limitations.

In addition to failing to disclose every limitation of the rejected claims, the Lennox and Anderson references together fail to provide the requisite motivation or suggestion to alter their teachings to provide "a capture probe nucleic acid covalently attached to said electrode." No teaching of the presently claimed subject matter is made in any of the cited references, and as

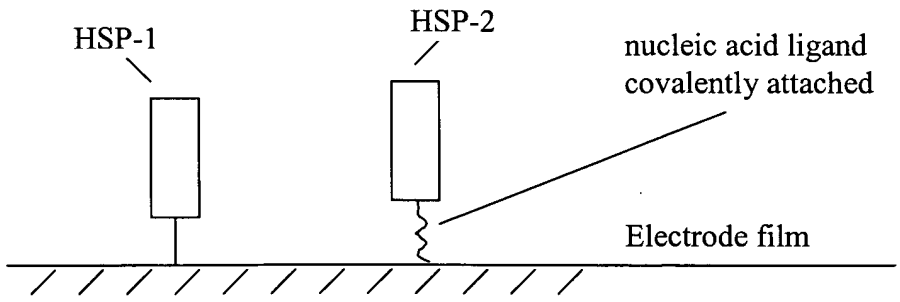
such the cited references as a whole fail to provide the requisite motivation or suggestion to make the claimed invention.

3. Modifying the cited references to make the claimed invention would impermissibly change the principle of operation of the primary Lennox reference.

A "proposed modification cannot change the principle of operation of a reference." MPEP § 2143.01. Moreover, "if a proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." MPEP § 2143.01.

In the present application, modifying Lennox to make a "capture probe nucleic acid covalently attached to said electrode" as claimed fundamentally changes the principle of operation of Lennox. Lennox discloses the HSP1 protein covalently attached to the electrode film. See Col. 8 lines 17-26. HSP2 is described as including an attached ligand which can be a nucleic acid. See Col. 8 lines 10-14 and lines 57-63. As disclosed and illustrated in Col. 10 lines 31-35 and Fig. 5A-B, the HSP2-containing ligand (59) is added to the covalently attached-HSP1 (58), resulting in binding of HSP1 and HSP2. This protein-protein interaction is dependent on a repeated heptad motif of conserved amino acid residues in each peptide's primary amino acid sequence. See Col. 6, lines 39-50.

If a person of ordinary skill in the art were to modify the HSP2 nucleic acid component so as to covalently attach it to the electrode film, Lennox's principle of operation would be impermissibly altered. Further, the method of detection would be inoperable. As discussed above, free HSP2 is added to the electrode-bound HSP1 to induce the formation of heterodimers through the HSP1/HSP2 interaction. If, as illustrated below, the nucleic acid portion of HSP2 is covalently attached to the electrode film, then HSP2 would not be able to form heterodimers with HSP1.



Lennox states that heterodimer formation enhances the close packed structure of the monolayer as shown by the drop in conductance in Fig. 7. See Col. 12 lines 13-19. Lennox discloses the importance of the role of the close packed monolayer in the operation of the biosensor:

> The triggering event in the biosensor is the binding of a ligand-binding agent to the surface-bound ligand. This binding perturbs the ordered structure of the monolayer sufficiently to allow the movement of redox species through the monolayer, producing current through the electrode. Measurements performed in support of the invention indicate that one triggering event leads to 10^2 to 10^6 ionic and electron transfer events per second, and thus is highly multiplicative. The biosensor records this binding event as an increase in current across the electrode, i.e., between the working and counter electrodes. See Col. 12 lines 51-61.

The covalent attachment of the HSP2 nucleic acid portion to the electrode would not allow heterodimer formation and consequently prevent the formation of a low conductance monolayer. Under such conditions, the binding of a ligand-binding agent to the HSP2 nucleic acid portion would be undetectable and binding events would not be recorded by the biosensor.

Additionally, such conditions would prevent ligand-binding agent interactions. As the nucleic acid portion of HSP2 serves as the ligand for the ligand-binding agent sought to be detected, its attachment to the electrode film, as shown above, would prevent it from binding any potential ligand-binding agents. Under such conditions, the monolayer structure would remain unperturbed and consequently the biosensor would not be triggered. Thus, modifying Lennox to make the claimed invention fundamentally changes the principle of operation of the cited reference. Because "the proposed modification cannot change the principle of operation of a reference," the references are not sufficient to render the claims prima facie obvious.

The Examiner has noted the above assertion is unpersuasive because Lennox "specifically teaches nucleic acid capture binding ligands." However, as previously discussed, the reference does not teach a "nucleic acid capture probe covalently attached" to an electrode as required by the claims.

4. The cited references fail to suggest that modifying their teachings would have a reasonable chance of success.

The references as a whole fail to provide a reasonable chance of success for making "a capture probe nucleic acid covalently attached to said electrode." No teaching of the claimed

subject matter is made in any of the cited references, and as such the cited references fail to provide a reasonable expectation of success to make the claimed invention.

For all the reasons cited above, The cited references in combination fail to render the claims obvious. Applicant respectfully request that this ground for rejection be withdrawn.

Conclusion

Applicants submit the claims are in condition for allowance, and notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,

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